

Kam 09/787,082

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(FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
13:02:08 ON 25 MAR 2003)

L16 33 DUP REM L15 (16 DUPLICATES REMOVED)

=> d que l16

L1 1063 SEA CRAIK D?/AU  
L2 513 SEA DALY N?/AU  
L3 5459 SEA NIELSEN K?/AU  
L4 6842 SEA (L1 OR L2 OR L3)  
L5 129 SEA L4 AND CONOTOXIN#  
L6 14 SEA L5 AND CYCL?  
L7 6 SEA L5 AND CIRC?  
L8 15 SEA L6 OR L7  
L9 21 SEA CONOTOXIN# (5A) CYCL?  
L10 32 SEA L8 OR L9  
L11 259 SEA CONOTOXIN?(5A) (DISULPHIDE# OR DISULFIDE#)  
L12 8 SEA L11 AND KNOT  
L13 40 SEA L10 OR L12  
L14 9 SEA CONOTOXIN?(10A) LINKER?  
L15 49 SEA L13 OR L14  
L16 33 DUP REM L15 (16 DUPLICATES REMOVED)

=> d ibib abs l16 1-33

L16 ANSWER 1 OF 33 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 1  
ACCESSION NUMBER: 2002:112596 HCAPLUS  
DOCUMENT NUMBER: 136:320633  
TITLE: Initial Disulfide Formation Steps in the Folding of an  
.omega.-Conotoxin  
AUTHOR(S): Price-Carter, Marian; Bulaj, Grzegorz; Goldenberg,  
David P.  
CORPORATE SOURCE: Department of Biology, University of Utah, Salt Lake  
City, UT, 84112-0840, USA  
SOURCE: Biochemistry (2002), 41(10), 3507-3519  
CODEN: BICHAW; ISSN: 0006-2960  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB To det. whether the native **disulfides** of .omega.-  
**conotoxins** are preferentially stabilized early in the folding of  
these small proteins, the rates and equil. for disulfide formation were  
measured for three analogs of .omega.-conotoxin MVIIA. In each analog,  
one of the three pairs of disulfide-bonded Cys residues was replaced with  
Ala residues, leaving four Cys residues that can form six intermediates  
with one disulfide and three species with two disulfides. For each  
analog, all of the disulfide-bonded species were identified, and the  
equil. consts. for forming the individual species via exchange with  
oxidized and reduced glutathione were measured. These equil. consts.  
represent effective concns. of the Cys thiols and ranged from 0.01 to 0.4  
M in the fully reduced protein. There was little or no preference for  
forming the native disulfides, and the equil. for forming the first and  
second disulfides decreased only slightly upon the addn. of 8 M urea. The  
data for the four-Cys analogs, together with equil. data for the six-Cys  
form, were also used to est. effective concns. for forming a third  
disulfide once two native disulfides are present. These effective concns.  
were approx. 100 and 10 M in the presence of 0 and 8 M urea, resp. The

results indicate that there is little or no preferential formation of native interactions in the folding of these mols. until two disulfides have formed, after which there is a high degree of cooperativity among the native interactions.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
2

ACCESSION NUMBER: 2002:221301 BIOSIS  
DOCUMENT NUMBER: PREV200200221301  
TITLE: **Circular** proteins: No end in sight.  
AUTHOR(S): Trabi, Manuela (1); **Craik, David J.**  
CORPORATE SOURCE: (1) Institute for Molecular Bioscience, University of Queensland, Brisbane, QLD, 4072: d.craik@imb.uq.edu.au Australia  
SOURCE: Trends in Biochemical Sciences, (March, 2002) Vol. 27, No. 3, pp. 132-138. <http://journals.bmn.com/journals/list/latest?jcode=tibs>. print.  
ISSN: 0968-0004.  
DOCUMENT TYPE: General Review  
LANGUAGE: English

AB **Circular** proteins are a recently discovered phenomenon. They presumably evolved to confer advantages over ancestral linear proteins while maintaining the intrinsic biological functions of those proteins. In general, these advantages include a reduced sensitivity to proteolytic cleavage and enhanced stability. In one remarkable family of **circular** proteins, the **cyclotides**, the **cyclic** backbone is additionally braced by a knotted arrangement of disulfide bonds that confers additional stability and topological complexity upon the family. This article describes the discovery, structure, function and biosynthesis of the currently known **circular** proteins. The discovery of naturally occurring **circular** proteins in the past few years has been complemented by new chemical and biochemical methods to make synthetic **circular** proteins; these are also briefly described.

L16 ANSWER 3 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:546059 BIOSIS  
DOCUMENT NUMBER: PREV200200546059  
TITLE: Controlling the cysteine framework of N to C **cyclic** analogues of alpha-**Conotoxin** ImI.  
AUTHOR(S): Armishaw, C. J. (1); Dutton, J. L. (1); Hogg, R. C.; Adams, D. J.; **Craik, D. J. (1)**; Alewood, P. F. (1)  
CORPORATE SOURCE: (1) Institute for Molecular Bioscience, The University of Queensland, Brisbane, QLD, 4072 Australia  
SOURCE: Journal of Peptide Science, (2002) Vol. 8, No. Supplement, pp. S78. <http://www.interscience.wiley.com/jpages/1075-2617/>. print.  
Meeting Info.: 27th European Peptide Symposium Sorrento, Italy August 31-September 06, 2002  
ISSN: 1075-2617.  
DOCUMENT TYPE: Conference  
LANGUAGE: English

L16 ANSWER 4 OF 33 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:692447 HCAPLUS  
TITLE: Antimicrobial and chemotactic activities of .omega.-**conotoxin cyclic** analogues

AUTHOR(S): Yang, Jin-Long; Lu, Yi-An; Wu, Chengwei; Tam, James P.  
 CORPORATE SOURCE: Department of Microbiology and Immunology, University of Vanderbilt, Nashville, TN, 37232, USA  
 SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 487-488. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif.  
 CODEN: 69DBAL; ISBN: 0-9715560-0-8  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

AB Three **cyclic** .omega.-**conotoxin** analogs were prepd. with different disulfide constraints to det. whether the open-chain .omega.-conotoxins are microbicidal and whether their activity can be improved by end-to-end cyclic analogs mimicking the plant macrocycles. The hemolytic and chemostatic activities of the .omega.-conotoxins were detd. attendant to membranolytic and defense mechanisms of antimicrobials. Solid-phase peptide synthesis method based on thia-zip cyclization was employed to synthesize 3 cyclic analogs cA1-cA3 based on .omega.-conotoxin MVIIA. Since the N- and C-termini of MVIIA are not spatially close, computer modeling showed that the end-to-end cyclization of the native MVIIA to cA1-cA3 imparts conformational changes even though their amino acid sequences are essentially similar. MVIIA was completely inactive against both Gram-neg. (E. coli) and Gram-pos. bacteria (Staphylococcus aureus) although it had marginally activity against fungi (C. kefyr). Analog cA1, a cyclized MVIIA with 2 disulfides displayed enhanced microbicidal activity against the 3 test organisms with MICs of 2-11 .mu.M. Reducing the conformational constraint of cA1 by replacing the Cys-15,25 disulfide by 2 Abu in cA2 lowered its potency 2-4-fold. Replacing the Cys-1,16 disulfide pair by Abu in cA3 also resulted in decreased antimicrobial activity compared to cA1 against S. aureus and C. kefyr, while activity against E. coli was retained. MVIIA and all 3 cyclic analogs showed low hemolytic activity and low toxicity on human erythrocytes. Chemotaxis based on monocyte migrations were cA1>cA3>cA2=MVIIA.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 33 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:692271 HCAPLUS  
 TITLE: Synthesis of N to C terminal **cyclic** analogues of .alpha.-**conotoxin** ImI by chemoselective ligation of unprotected linear precursors  
 AUTHOR(S): Armishaw, Christopher J.; Dutton, Julie; Hogg, Ron C.; Adams, David J.; **Craik, David J.**; Alewood, Paul F.  
 CORPORATE SOURCE: Institute for Molecular Bioscience, The University of Queensland, Brisbane, Queensland, 4072, Australia  
 SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 113-114. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif.  
 CODEN: 69DBAL; ISBN: 0-9715560-0-8  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

AB The hypothesis that N to C terminal **cyclization** of ImI with insertion of a single amino acid or dipeptide space would further enhance its stability and potentially its bioavailability with minimal disruption to the native ImI structure was tested using two **cyclic** ImI analogs, cImI-A and cImI-AG. The two acyclic conopeptides were synthesized using a one-pot native chem. ligation strategy as the target mols. contain a convenient Gly-Cys ligation site. Following purifn., a series of trial **cyclizations** were attempted under various conditions. For both analogs, 0.1 M Tris + 2 M Gn.cntdot.HCl, pH 8.4 were most effective. CImI-AG displayed a mixt. of disulfide isomers in approx. 1:4:1 ratios, whereas cImI-A displayed one major isomer. The major product of each expt. was isolated and further characterized.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 33 SCISEARCH COPYRIGHT 2003 ISI (R)  
 ACCESSION NUMBER: 2000:696114 SCISEARCH  
 THE GENUINE ARTICLE: 352KW  
 TITLE: The cystine knot motif in toxins and implications for drug design  
 AUTHOR: Craik D J (Reprint); Daly N L; Waine C  
 CORPORATE SOURCE: UNIV QUEENSLAND, CTR DRUG DESIGN & DEV, INST MOL BIOSCI, BRISBANE, QLD 4072, AUSTRALIA (Reprint)  
 COUNTRY OF AUTHOR: AUSTRALIA  
 SOURCE: TOXICON, (JAN 2001) Vol. 39, No. 1, pp. 43-60.  
 Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.  
 ISSN: 0041-0101.  
 DOCUMENT TYPE: Article; Journal  
 FILE SEGMENT: LIFE  
 LANGUAGE: English  
 REFERENCE COUNT: 69

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB The cystine knot structural motif is present in peptides and proteins from a variety of species, including fungi, plants, marine molluscs, insects and spiders. It comprises an embedded ring formed by two disulfide bonds and their connecting backbone segments which is threaded by a third disulfide bond. It is invariably associated with nearby beta-sheet structure and appears to be a highly efficient motif for structure stabilization. Because of this stability it makes an ideal framework for molecular engineering applications. In this review we summarize the main structural features of the cystine knot motif, focussing on toxin molecules containing either the inhibitor cystine knot or the **cyclic** cystine knot. Peptides containing these motifs are 26-48 residues long and include ion channel blockers, haemolytic agents, as well as molecules having antiviral and antibacterial activities. The stability of peptide toxins containing the cystine knot motif, their range of bioactivities and their unique structural scaffold can be harnessed for molecular engineering applications and in drug design. Applications of cystine knot molecules for the treatment of pain. and their potential use in antiviral and antibacterial applications are described. (C) 2000 Elsevier Science Ltd. All rights reserved.

L16 ANSWER 7 OF 33 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2000:191100 HCAPLUS  
 DOCUMENT NUMBER: 132:237373  
 TITLE: Preparation of **cyclized** conotoxin peptides  
 INVENTOR(S): Craik, David James; Daly, Norelle

PATENT ASSIGNEE(S): **Lee; Nielsen, Katherine Justine**  
 SOURCE: University of Queensland, Australia  
 PCT Int. Appl., 43 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015654	A1	20000323	WO 1999-AU769	19990914
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960705	A1	20000403	AU 1999-60705	19990914
AU 747006	B2	20020509		
EP 1129106	A1	20010905	EP 1999-947111	19990914
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			AU 1998-5895	A 19980914
			WO 1999-AU769	W 19990914

AB **Cyclized conotoxin** peptides were prepd. for the  
 therapeutic treatment of mammals. Thus, **cyclo**  
 [CKGKGAKCSRLMYDCCTGSCRSKGKCTRNGLPG], a **cyclic** analog of MVIIA  
 having the linking moiety TRNGLPG, was prepd. by the solid-phase method.  
 REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 33 MEDLINE DUPLICATE 3  
 ACCESSION NUMBER: 2001081139 MEDLINE  
 DOCUMENT NUMBER: 20552922 PubMed ID: 11101291  
 TITLE: Three-dimensional solution structure of omega-conotoxin  
 TxVII, an L-type calcium channel blocker.  
 AUTHOR: Kobayashi K; Sasaki T; Sato K; Kohno T  
 CORPORATE SOURCE: Mitsubishi Kasei Institute of Life Sciences, Minamiooya,  
 Machida, Tokyo 194-8511, Japan.  
 SOURCE: BIOCHEMISTRY, (2000 Dec 5) 39 (48) 14761-7.  
 Journal code: 0370623. ISSN: 0006-2960.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200101  
 ENTRY DATE: Entered STN: 20010322  
 Last Updated on STN: 20010322  
 Entered Medline: 20010105

AB We determined the three-dimensional structure of omega-conotoxin TxVII, a  
 26-residue peptide that is an L-type calcium channel blocker, by (1)H NMR  
 in aqueous solution. Twenty converged structures of this peptide were  
 obtained on the basis of 411 distance constraints obtained from nuclear  
 Overhauser effect connectivities, 20 torsion angle constraints, and 21  
 constraints associated with hydrogen bonds and disulfide bonds. The

root-mean-square deviations about the averaged coordinates of the backbone atoms (N, C(alpha), C, and O) and all heavy atoms were 0.50 +/- 0.09 A and 0.99 +/- 0.13 A, respectively. The structure of omega-conotoxin TxVII is composed of a triple-stranded antiparallel beta-sheet and four turns. The three **disulfide** bonds in omega-conotoxin TxVII form the classical cystine **knot** motif of toxic or inhibitory polypeptides. The overall folding of omega-conotoxin TxVII is similar to those of the N-type calcium channel blockers, omega-conotoxin GVIA and MVIIA, despite the low amino acid sequence homology among them. omega-Conotoxin TxVII exposes many hydrophobic residues to a certain surface area. In contrast, omega-conotoxin GVIA and MVIIA expose basic residues in the same way as omega-conotoxin TxVII. The channel binding site of omega-conotoxin TxVII is different from those of omega-conotoxin GVIA and MVIIA, although the overall folding of these three peptides is similar. The gathered hydrophobic residues of omega-conotoxin TxVII probably interact with the hydrophobic cluster of the alpha(1) subunit of the L-type calcium channel, which consists of 13 residues located in segments 5 and 6 in domain III and in segment 6 in domain IV.

L16 ANSWER 9 OF 33 SCISEARCH COPYRIGHT 2003 ISI (R)  
 ACCESSION NUMBER: 2000:110058 SCISEARCH  
 THE GENUINE ARTICLE: 274RR  
 TITLE: Charged residues in P-S6 **linkers** critical for mu-**conotoxin** block or rat skeletal muscle Na channel pore.  
 AUTHOR: Li R A (Reprint); Velez P; Tomaselli G F; Marban E  
 CORPORATE SOURCE: JOHNS HOPKINS UNIV, SCH MED, BALTIMORE, MD 21205  
 COUNTRY OF AUTHOR: USA  
 SOURCE: BIOPHYSICAL JOURNAL, (JAN 2000) Vol. 78, No. 1, Part 2, pp. PO511-PO511.  
 Publisher: BIOPHYSICAL SOCIETY, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.  
 ISSN: 0006-3495.  
 DOCUMENT TYPE: Conference; Journal  
 FILE SEGMENT: LIFE  
 LANGUAGE: English  
 REFERENCE COUNT: 0

L16 ANSWER 10 OF 33 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2000:323977 HCAPLUS  
 DOCUMENT NUMBER: 133:148851  
 TITLE: Synthesis and antibody recognition of mucin 1 (MUC1)-.alpha.-conotoxin chimera  
 AUTHOR(S): Drakopoulou, Eugenia; Uray, Katalin; Mezo, Gabor; Price, Michael R.; Vita, Claudio; Hudecz, Ferenc  
 CORPORATE SOURCE: Departement d'Ingenierie et d'Etudes des Proteines, CEA, Gif-sur-Yvette, Fr.  
 SOURCE: Journal of Peptide Science (2000), 6(4), 175-185  
 CODEN: JPSIEI; ISSN: 1075-2617  
 PUBLISHER: John Wiley & Sons Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The authors synthesized and characterized new chimera peptides by inserting an epitope of the mucin 1 glycoprotein (MUC1) as a "guest" sequence in the "host" structure of .alpha.-conotoxin GI, a 13-residue peptide (ECCNPACGRHYSC) isolated from the venom of Conus geographus. The Pro-Asp-Thr-Arg (PDTR) sequence of MUC1 selected for these studies is highly hydrophilic and adopts a .beta.-turn conformation. The .alpha.-conotoxin GI also contains a .beta.-turn in the 8-12 region, which

is stabilized by two disulfide bridges in positions 2-7 and 3-13. Thus, the tetramer sequence of .alpha.-conotoxin, Arg9-His-Tyr-Ser12, has been replaced by PDTR, comprising the minimal epitope for MUC1 specific monoclonal antibodies (MAbs) HMFG1 (PDTR) and HMFG2 (DTR). Synthesis of the chimera peptide was carried out by Fmoc strategy on (4-(2',4'-dimethoxyphenyl-aminomethyl)phenoxy) (Rink) resin and either 5,5'-dithio-bis(2-nitrobenzoic acid) (DTNB) or air oxidn. was applied for the formation of the first Cys3-Cys13 or Cys2-Cys7 disulfide bridge, resp. For the second disulfide bridge, three different oxidn. procedures (iodine in acetic acid, 10% DMSO/1 M HCl or tallium trifluoroacetate (Tl(tfa)3) in TFA) were utilized. The HPLC purified peptides were characterized by electrospray mass spectrometry (ES-MS) and amino acid anal. The CD spectra of the bicyclic MUC1-.alpha.-[Tyr1]-conotoxin chimera peptide showed partially ordered conformation with turn character. In antibody binding studies, the RIA data showed that both the linear and the bicyclic forms of MUC1-.alpha.-[Tyr1]-conotoxin chimera were recognized by MAb HMFG1 specific for PDTR sequence, while no binding was obsd. between MAb HMFG2 and various forms of the chimera. MAb HMFG1, using synthetic epitope conjugates or native MUC1 as target antigens, recognizes the PDTR motif more efficiently in the linear than in the bicyclic compd., but no reactivity was found with the monocyclic forms of MUC1-.alpha.-[Tyr1]-conotoxin chimera, underlining the importance of certain conformers stabilized by double cyclization.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 11 OF 33 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 4

ACCESSION NUMBER: 2000:536126 HCAPLUS

DOCUMENT NUMBER: 133:292127

TITLE: The cyclic contryphan motif CPxXPXC, a robust scaffold potentially useful as an .omega.-conotoxin mimic

AUTHOR(S): Pallaghy, Paul K.; Norton, Raymond S.

CORPORATE SOURCE: Biomolecular Research Institute, Parkville, 3052, Australia

SOURCE: Biopolymers (2000), 54(3), 173-179

CODEN: BIPMAA; ISSN: 0006-3525

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Contryphan-R, from venom of the cone-shell *Conus radiatus*, represents a novel cyclic peptide scaffold onto which residues may be grafted to mimic unrelated protein surfaces. Three substitutions were made at the x and X positions of the disulfide-bridged motif CPxXPXC, where X and x represent any L- and D-handed residues, resp., P represents proline or hydroxyproline, and C a half-cystine. These substitutions were designed to mimic part of the pharmacophore of the unrelated globular polypeptide .omega.-conotoxin GVIA, which blocks N-type calcium channels. The structure of this engineered contryphan, YNK-contryphan-R ([DTyr 4, Asn 5, Lys 7]contryphan-R), is shown to be similar to that of native contryphan-R, confirming that the scaffold is robust with respect to the multiple substitutions. In particular, the .alpha.-.beta. bond vectors characterizing the orientation of the side chains relative to the backbone are similar in contryphan-R, YNK-contryphan-R, and .omega.-conotoxin GVIA, which is the required result for a scaffold-based approach to mol. design. The soln. structure of YNK-contryphan-R has an N-terminal, nonhydrogen-bonded, chain reversal centered on Hyp 3-DTrp 4, and a C-terminal type 1 .beta.-turn. A minor form due to cis-trans isomerism of the Hyp2Cys 3 peptide bond is present in YNK-contryphan-R in a larger proportion than in contryphan-R. It is evident, particularly from the

3JH.alpha.HN coupling consts., that YNK-contryphan-R is more flexible than contryphan-R, probably due to the absence in YNK-contryphan-R of the Pro-Trp packing present in the native mol. Nevertheless, the structure confirms that cyclic peptide mol. can achieve the intended conformations.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 12 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:153502 BIOSIS

DOCUMENT NUMBER: PREV200000153502

TITLE: Charged residues in P-S6 **linkers** critical for mu-**conotoxin** block of rat skeletal muscle Na channel pore.

AUTHOR(S): Li, Ronald A. (1); Velez, P. (1); Tomaselli, G. F. (1); Marban, E. (1)

CORPORATE SOURCE: (1) The Johns Hopkins University School of Medicine, Baltimore, MD, 21205 USA

SOURCE: Biophysical Journal., (Jan., 2000) Vol. 78, No. 1 Part 2, pp. 87A.

Meeting Info.: 44th Annual Meeting of the Biophysical Society. New Orleans, Louisiana, USA February 12-16, 2000  
ISSN: 0006-3495.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

L16 ANSWER 13 OF 33 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000288969 EMBASE

TITLE: The cystine knot motif in toxins and implications for drug design.

AUTHOR: **Craik D.J.; Daly N.L.;** Wayne C.

CORPORATE SOURCE: D.J. Craik, Centre for Drug Design/Development, Institute for Molecular Bioscience, University of Queensland, Brisbane, QLD 4072, Australia. d.craik@mailbox.uq.edu.au

SOURCE: Toxicon, (1 Jan 2001) 39/1 (43-60).

Refs: 69

ISSN: 0041-0101 CODEN: TOXIA6

PUBLISHER IDENT.: S 0041-0101(00)00160-4

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 030 Pharmacology

037 Drug Literature Index

052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The cystine knot structural motif is present in peptides and proteins from a variety of species, including fungi, plants, marine molluscs, insects and spiders. It comprises an embedded ring formed by two disulfide bonds and their connecting backbone segments which is threaded by a third disulfide bond. It is invariably associated with nearby .beta.-sheet structure and appears to be a highly efficient motif for structure stabilization. Because of this stability it makes an ideal framework for molecular engineering applications. In this review we summarize the main structural features of the cystine knot motif, focussing on toxin molecules containing either the inhibitor cystine knot or the **cyclic** cystine knot. Peptides containing these motifs are 26-48 residues long and include ion channel blockers, haemolytic agents, as well as molecules having antiviral and antibacterial activities. The stability of peptide toxins containing the cystine knot motif, their range of



bioactivities and their unique structural scaffold can be harnessed for molecular engineering applications and in drug design. Applications of cystine knot molecules for the treatment of pain, and their potential use in antiviral and antibacterial applications are described. (C) 2000 Elsevier Science Ltd.

L16 ANSWER 14 OF 33 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:799423 HCAPLUS  
DOCUMENT NUMBER: 132:194650  
TITLE: Controlled syntheses of natural and disulfide-mispaired regioisomers of .alpha.-conotoxin SI  
AUTHOR(S): Hargittai, B.; Barany, G.  
CORPORATE SOURCE: Department of Chemistry, University of Minnesota, Minneapolis, MN, 55455-0431, USA  
SOURCE: Journal of Peptide Research (1999), 54(6), 468-479  
CODEN: JPERFA; ISSN: 1397-002X  
PUBLISHER: Munksgaard International Publishers Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Methods are reported for the unambiguous syntheses of all three possible disulfide regioisomers with the sequence of .alpha.-conotoxin SI, a tridecapeptide amide from marine cone snail venom that binds selectively to the muscle subtype of nicotinic acetylcholine receptors. The naturally occurring peptide has two "interlocking" disulfide bridges connecting Cys2-Cys7 and Cys3-Cys13 (2/7 & 3/13), while in the two mispaired isomers the disulfide bridges connect Cys2-Cys13 and Cys3-Cys7 (2/13 & 3/7, "nested") and Cys2-Cys3 and Cys7-Cys13 (2/3 & 7/13, "discrete"), resp. Alignment of disulfide bridges was controlled at the level of orthogonal protection schemes for the linear precursors, assembled by Fmoc solid-phase peptide synthesis on acidolyzable tris(alkoxy)benzylamide (PAL) supports. Side-chain protection of cysteine was provided by suitable pairwise combination of the S-9H-xanthen-9-yl (Xan) and S-acetamidomethyl (Acm) protecting groups. The first disulfide bridge was formed from the corresponding bis(thiol) precursor obtained by selective deprotection of S-Xan, and the second disulfide bridge was formed by orthogonal co-oxidn. of S-Acm groups on the remaining two Cys residues. It was possible to achieve the desired alignments with either order of loop formation (smaller loop before larger, or vice versa). The highest overall yields were obtained when both disulfides were formed in soln., while expts. where either the first or both bridges were formed while the peptide was on the solid support revealed lower overall yields and poorer selectivities towards the desired isomers.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 15 OF 33 MEDLINE

ACCESSION NUMBER: 1999143291 MEDLINE  
DOCUMENT NUMBER: 99143291 PubMed ID: 9986713  
TITLE: Structure-activity studies of conantokins as human N-methyl-D-aspartate receptor modulators.  
AUTHOR: Nielsen K J; Skjaerbaek N; Dooley M; Adams D A; Mortensen M; Dodd P R; Craik D J; Alewood P F; Lewis R J  
CORPORATE SOURCE: Centre for Drug Design and Development, The University of Queensland, Brisbane, Queensland 4072, Australia.  
SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (1999 Feb 11) 42 (3) 415-26.  
Journal code: 9716531. ISSN: 0022-2623.

PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199903  
 ENTRY DATE: Entered STN: 19990326  
 Last Updated on STN: 19990326  
 Entered Medline: 19990316

AB The activities of conantokin-G (con-G), conantokin-T (con-T), and several novel analogues have been studied using polyamine enhancement of [3H]MK-801 binding to human glutamate-N-methyl-D-aspartate (NMDA) receptors, and their structures have been examined using CD and 1H NMR spectroscopy. The potencies of con-G[A7], con-G, and con-T as noncompetitive inhibitors of spermine-enhanced [3H]MK-801 binding to NMDA receptor obtained from human brain tissue are similar to those obtained using rat brain tissue. The secondary structure and activity of con-G are found to be highly sensitive to amino acid substitution and modification. NMR chemical shift data indicate that con-G, con-G[D8, D17], and con-G[A7] have similar conformations in the presence of Ca<sup>2+</sup>. This consists of a helix for residues 2-16, which is kinked in the vicinity of Glu10. This is confirmed by 3D structure calculations on con-G[A7]. Restraining this helix in a linear form (i.e., con-G[A7,E10-K13]) results in a minor reduction in potency. Incorporation of a 7-10 salt-bridge replacement (con-G[K7-E10]) prevents helix formation in aqueous solution and produces a peptide with low potency. Peptides with the Leu5-Tyr5 substitution also have low potencies (con-G[Y5,A7] and con-G[Y5,K7]) indicating that Leu5 in con-G is important for full antagonist behavior. We have also shown that the Glu-Ala7 substitution increases potency, whereas the Glu-Lys7 substitution has no effect. Con-G and con-G[K7] both exhibit selectivity between NMDA subtypes from mid-frontal and superior temporal gyri, but not between sensorimotor and mid-frontal gyri. Asn8 and/or Asn17 appear to be important for the ability of con-G to function as an inhibitor of polyamine-stimulated [3H]MK-801 binding, but not in maintaining secondary structure. The presence of Ca<sup>2+</sup> does not increase the potencies of con-G and con-T for NMDA receptors but does stabilize the helical structures of con-G, con-G[D8,D17], and, to a lesser extent, con-G[A7]. The NMR data support the existence of at least two independent Ca<sup>2+</sup>-chelating sites in con-G, one involving Glu7 and possibly Glu3 and the other likely to involve Glu10 and/or Glu14.

L16 ANSWER 16 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:66958 BIOSIS  
 DOCUMENT NUMBER: PREV200000066958

TITLE: A single amino acid substitution in the alpha1B calcium channel domain III S5-S6 **linker** increases affinity and reversibility for omega-**conotoxin** GVIA.

AUTHOR(S): Feng, Z.-P. (1); Bosey, G. R.; Snutch, T. P.; Zamponi, G. W. (1)

CORPORATE SOURCE: (1) Department of Pharmacology and Therapeutics, University of Calgary, Calgary, AB Canada

SOURCE: Society for Neuroscience Abstracts, (1999) Vol. 25, No. 1-2, pp. 194.  
 Meeting Info.: 29th Annual Meeting of the Society for Neuroscience, Part 1 Miami Beach, Florida, USA October 23-28, 1999 The Society for Neuroscience  
 . ISSN: 0190-5295.

DOCUMENT TYPE: Conference  
 LANGUAGE: English

L16 ANSWER 17 OF 33 SCISEARCH COPYRIGHT 2003 ISI (R)  
ACCESSION NUMBER: 1999:739170 SCISEARCH  
THE GENUINE ARTICLE: 239FY  
TITLE: Role of disulfide bridges in the folding, structure and  
biological activity of omega-conotoxin GVIA  
AUTHOR: Flinn J P; Pallaghy P K; Lew M J; Murphy R; Angus J A;  
Norton R S (Reprint)  
CORPORATE SOURCE: BIOMOL RES INST, 343 ROYAL PARADE, PARKVILLE, VIC 3052,  
AUSTRALIA (Reprint); BIOMOL RES INST, PARKVILLE, VIC 3052,  
AUSTRALIA; UNIV MELBOURNE, DEPT PHARMACOL, PARKVILLE, VIC  
3052, AUSTRALIA  
COUNTRY OF AUTHOR: AUSTRALIA  
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA-PROTEIN STRUCTURE AND  
MOLECULAR ENZYMOLOGY, (14 SEP 1999) Vol. 1434, No. 1, pp.  
177-190.  
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE  
AMSTERDAM, NETHERLANDS.  
ISSN: 0167-4838.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 41

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB      omega-Conotoxin GVIA (GVIA), an N-type calcium channel blocker from the  
cone shell *Conus geographus*, is a 27 residue polypeptide cross-linked by  
three disulfide bonds. Here, we report the synthesis, structural analysis  
by H-1 NMR and bioassay of analogues of GVIA with disulfide bridge  
deletions and N- and C-terminal truncations. Two analogues that retain the  
crucial Lys-2 and Tyr-13 residues in loops constrained by two native  
disulfide bridges were synthesised using orthogonal protection of cysteine  
residues. In the first analogue, the Cys-15-Cys-26 disulfide bridge was  
deleted (by replacing the appropriate Cys residues with Ser), while in the  
second, this disulfide bridge and the eight C-terminal residues were  
deleted. No activity was detected for either analogue in a rat vas  
deferens assay, which measures N-type calcium channel activity in  
sympathetic nerve, and NMR studies showed that this was due to a gross  
loss of secondary and tertiary structure. Five inactive analogues that  
were synthesised without orthogonal protection of Cys residues as part of  
a previous study (Flinn et al. (1995) J. Pept. Sci. 1, 379-384) were also  
investigated. Three had single disulfide deletions (via Ser substitutions)  
and two had N- or C-terminal deletions in addition to the disulfide  
deletion. Peptide mapping and NMR analyses demonstrated that at least four  
of these analogues had non-native disulfide pairings, which presumably  
accounts for their lack of activity. The NMR studies also showed that all  
five analogues had substantially altered tertiary structures, although the  
backbone chemical shifts and nuclear Overhauser enhancements (NOEs)  
implied that native-like turn structures persisted in some of these  
analogues despite the non-native disulfide pairings. This work  
demonstrates the importance of the **disulfides** in omega-  
**conotoxin** folding and shows that the Cys-15-Cys-26 disulfide is  
essential for activity in GVIA. The NMR analyses also emphasise that  
backbone chemical shifts and short- and medium-range NOEs are dictated  
largely by local secondary structure elements and are not necessarily  
reliable monitors of the tertiary fold. (C) 1999 Elsevier Science B.V. All  
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L16 ANSWER 18 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 1999:16695 BIOSIS

DOCUMENT NUMBER: PREV199900016695  
 TITLE: Three-dimensional solution structure of alpha-**conotoxin** MII by NMR spectroscopy: Effects of solution environment on helicity.  
 AUTHOR(S): Hill, Justine M.; Oomen, Clasien J.; Miranda, Les P.; Bingham, Jon-Paul; Alewood, Paul F.; **Craik, David J.**  
 (1)  
 CORPORATE SOURCE: (1) Centre Drug Design Dev., Univ. Queensland, Brisbane, QLD 4072 Australia  
 SOURCE: Biochemistry, (Nov. 10, 1998) Vol. 37, No. 45, pp. 15621-15630.  
 ISSN: 0006-2960.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 AB **alpha-Conotoxin** MII, a 16-residue polypeptide from the venom of the piscivorous cone snail *Conus magus*, is a potent and highly specific blocker of mammalian neuronal nicotinic acetylcholine receptors composed of alpha3beta2 subunits. The role of this receptor type in the modulation of neurotransmitter release and its relevance to the problems of addiction and psychosis emphasize the importance of a structural understanding of the mode of interaction of MII with the alpha3beta2 interface. Here we describe the three-dimensional solution structure of MII determined using 2D 1H NMR spectroscopy. Structural restraints consisting of 376 interproton distances inferred from NOEs and 12 dihedral restraints derived from spin-spin coupling constants were used as input for simulated annealing calculations and energy minimization in the program X-PLOR. The final set of 20 structures is exceptionally well-defined with mean pairwise rms differences over the whole molecule of 0.07 ANG for the backbone atoms and 0.34 ANG for all heavy atoms. MII adopts a compact structure incorporating a central segment of alpha-helix and beta-turns at the N- and C-termini. The molecule is stabilized by two disulfide bonds, which provide cross-links between the N-terminus and both the middle and C-terminus of the structure. The susceptibility of the structure to conformational change was examined using several different solvent conditions. While the global fold of MII remains the same, the structure is stabilized in a more hydrophobic environment provided by the addition of acetonitrile or trifluoroethanol to the aqueous solution. The distribution of amino acid side chains in MII creates distinct hydrophobic and polar patches on its surface that may be important for the specific interaction with the alpha3beta2 neuronal nAChR. A comparison of the structure of MII with other neuronal-specific **alpha-conotoxins** provides insights into their mode of interaction with these receptors.

L16 ANSWER 19 OF 33 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1999:11026 HCAPLUS  
 DOCUMENT NUMBER: 130:177281  
 TITLE: Stimulation of airway sensory nerves by cyclosporin A and FK506 in guinea pig isolated bronchus  
 AUTHOR(S): Harrison, S.; Reddy, S.; Page, C. P.; Spina, D.  
 CORPORATE SOURCE: The Sackler Institute of Pulmonary Pharmacology, Department of Respiratory Medicine, King's College School of Medicine and Dentistry, London, SE5 9PJ, UK  
 SOURCE: British Journal of Pharmacology (1998), 125(7), 1405-1412  
 CODEN: BJPCBM; ISSN: 0007-1188  
 PUBLISHER: Stockton Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB We have investigated the contractile property of cyclosporin A and FK506

in guinea-pig isolated bronchus. Cyclosporin A failed to significantly attenuate the excitatory non-adrenergic non-cholinergic (eNANC) and cholinergic contractile response (per cent methacholine Emax) induced by elec. field stimulation (EFS). In contrast, eNANC responses were significantly attenuated by both the neurokinin (NK)-1 and (NK)-2 receptor antagonists, N-acetyl-L-tryptophan 3,5-bis (trifluoromethyl)-benzyl and SR48968, resp. Cyclosporin A and FK506 caused a concn.-dependent contraction in guinea-pig isolated bronchus, which was significantly attenuated by NK-1 and NK-2 receptor antagonists. The capsaicin receptor antagonist, capsazepine (10 .mu.M) significantly reduced the contractile response to cyclosporin A and capsaicin, but not to FK506. The N-type calcium channel blocker, .omega.-Contoxin (.omega.CTX: 10 nM), significantly reduced the contractile response to FK506 and the eNANC response following EFS. In contrast, .omega.-CTX failed to significantly reduce the contractile potency to capsaicin or cyclosporin A. In bronchial preps. desensitized by repeated application of capsaicin (1 .mu.M), the contractile responses to both cyclosporin A (100 .mu.M) and FK506 (100 .mu.M), were significantly reduced. In contrast, the contractile responses to substance P and neurokinin A (10 .mu.M) were not altered. Furthermore, repeated application of cyclosporin A (100 .mu.M) significantly inhibited the contractile response to capsaicin (1 .mu.M). The findings from this study would indicate that cyclosporin A and FK506 mediate contraction of guinea-pig isolated bronchus secondary to the release of neuropeptides from airway sensory nerves. However, the release of sensory neuropeptides appears to be mediated via different mechanisms for cyclosporin A and FK506, the former by stimulation of the vanilloid receptor and the latter via opening of N-type calcium channels.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 33 MEDLINE

ACCESSION NUMBER: 1998239743 MEDLINE  
DOCUMENT NUMBER: 98239743 PubMed ID: 9571060  
TITLE: Structure determination of the three disulfide bond isomers of alpha-conotoxin GI: a model for the role of disulfide bonds in structural stability.  
AUTHOR: Gehrman J; Alewood P F; Craik D J  
CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, QLD 4072, Australia.  
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1998 May 1) 278 (2) 401-15. Journal code: 2985088R. ISSN: 0022-2836.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199806  
ENTRY DATE: Entered STN: 19980713  
Last Updated on STN: 19980713  
Entered Medline: 19980630

AB The three possible disulfide bonded isomers of alpha-conotoxin GI have been selectively synthesised and their structures determined by 1H NMR spectroscopy. alpha-Conotoxin GI derives from the venom of Conus geographus and is a useful neuropharmacological tool as it selectively binds to the nicotinic acetylcholine receptor (nAChR), a ligand-gated ion channel involved in nerve signal transmission. The peptide has the sequence ECCNPACGRHYSC-NH2, and the three disulfide bonded isomers are referred to as GI(2-7;3-13), GI(2-13;3-7) and GI(2-3;7-13). The NMR structure for the native isomer GI(2-7;3-13) is of excellent quality, with a backbone pairwise RMSD of 0.16 A for a family of 35

structures, and comprises primarily a distorted 310 helix between residues 5 to 11. The two non-native isomers exhibit multiple conformers in solution, with the major populated forms being different in structure both from each other and from the native form. Structure-activity relationships for the native GI(2-7;3-13) as well as the role of the disulfide bonds on folding and stability of the three isomers are examined. It is concluded that the disulfide bonds in alpha-**conotoxin** GI play a crucial part in determining both the structure and stability of the peptide. A trend for increased conformational heterogeneity was observed in the order of GI(2-7;3-13) < GI(2-13;3-7) < GI(2-3;7-13). It was found that the peptide bond joining Cys2 to Cys3 in GI(2-3;7-13) is predominantly trans, rather than cis as theoretically predicted. These structural data are used to interpret the varying nAChR binding of the non-native forms. A model for the binding of native GI(2-7;3-13) to the mammalian nAChR is proposed, with an alpha-subunit binding face made up of Cys2, Asn4, Pro5, Ala6 and Cys7 and a selectivity face, comprised of Arg9 and His10. These two faces orient the molecule between the alpha and delta subunits of the receptor. The structure of the CCNPAC sequence of the native GI(2-7;3-13) is compared to the structure of the identical sequence from the toxic domain of heat-stable enterotoxins, which forms part of the receptor binding region of the enterotoxins, but which has a different disulfide connectivity.

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L16 ANSWER 21 OF 33 MEDLINE  
 ACCESSION NUMBER: 97444322 MEDLINE  
 DOCUMENT NUMBER: 97444322 PubMed ID: 9298951  
 TITLE: Crystal structure at 1.1 A resolution of alpha-**conotoxin** PnIB: comparison with alpha-**conotoxins** PnIA and GI.  
 AUTHOR: Hu S H; Gehrmann J; Alewood P F; **Craik D J**; Martin J L  
 CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, QLD 4072 Australia.  
 SOURCE: BIOCHEMISTRY, (1997 Sep 23) 36 (38) 11323-30.  
 Journal code: 0370623. ISSN: 0006-2960.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: PDB-1AKG  
 ENTRY MONTH: 199710  
 ENTRY DATE: Entered STN: 19971024  
 Last Updated on STN: 19971024  
 Entered Medline: 19971016  
 AB **Conotoxins** are small, cysteine-rich peptides isolated from the venom of *Conus* spp. of predatory marine snails, which selectively target specific receptors and ion channels critical to the functioning of the neuromuscular system. alpha-**Conotoxins** PnIA and PnIB are both 16-residue peptides (differing in sequence at only two positions) isolated from the molluscivorous snail *Conus pennaceus*. In contrast to the muscle-selective alpha-**conotoxin** GI from *Conus geographus*, PnIA and PnIB block the neuronal nicotinic acetylcholine receptor (nAChR). Here, we describe the crystal structure of PnIB, solved at a resolution of 1.1 A and phased using the Shake-and-Bake direct methods program. PnIB crystals are orthorhombic and belong to the space group P212121 with the following unit cell dimensions: a = 14.6 A, b = 26.1 A, and c = 29.2 A. The final refined structure of alpha-**conotoxin** PnIB includes all 16 residues plus 23 solvent molecules and has an overall R-factor of 14.7%

(R-free of 15.9%). The crystal structures of the alpha-conotoxins PnIB and PnIA are solved from different crystal forms, with different solvent contents. Comparison of the structures reveals them to be very similar, showing that the unique backbone and disulfide architecture is not strongly influenced by crystal lattice constraints or solvent interactions. This finding supports the notion that this structural scaffold is a rigid support for the presentation of important functional groups. The structures of PnIB and PnIA differ in their shape and surface charge distribution from that of GI.

L16 ANSWER 22 OF 33 MEDLINE  
 ACCESSION NUMBER: 97153002 MEDLINE  
 DOCUMENT NUMBER: 97153002 PubMed ID: 8999936  
 TITLE: Determination of the solution structures of conantokin-G and conantokin-T by CD and NMR spectroscopy.  
 AUTHOR: Skjaerbaek N; Nielsen K J; Lewis R J; Alewood P; Craik D J  
 CORPORATE SOURCE: The Centre for Drug Design and Development, The University of Queensland, Brisbane, Qld 4072, Australia.  
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Jan 24) 272 (4) 2291-9.  
 Journal code: 2985121R. ISSN: 0021-9258.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: PDB-1ONT; PDB-1ONU  
 ENTRY MONTH: 199702  
 ENTRY DATE: Entered STN: 19970306  
 Last Updated on STN: 19970306  
 Entered Medline: 19970221

AB Conantokin-G and conantokin-T are two paralytic polypeptide toxins originally isolated from the venom of the fish-hunting cone snails of the genus Conus. Conantokin-G and conantokin-T are the only naturally occurring peptidic compounds which possess N-methyl-D-aspartate receptor antagonist activity, produced by a selective non-competitive antagonism of polyamine responses. They are also structurally unusual in that they contain a disproportionately large number of acid labile post-translational gamma-carboxyglutamic acid (Gla) residues. Although no precise structural information has previously been published for these peptides, early spectroscopic measurements have indicated that both conantokin-G and conantokin-T form alpha-helical structures, although there is some debate whether the presence of calcium ions is required for these peptides to adopt this fold. We now report a detailed structural study of synthetic conantokin-G and conantokin-T in a range of solution conditions using CD and 1H NMR spectroscopy. The three-dimensional structures of conantokin-T and conantokin-G were calculated from 1H NMR-derived distance and dihedral restraints. Both conantokins were found to contain a mixture of alpha- and 310 helix, that give rise to curved and straight helical conformers. Conantokin-G requires the presence of divalent cations (Zn2+, Ca2+, Cu2+, or Mg2+) to form a stable alpha-helix, while conantokin-T adopts a stable alpha-helical structure in aqueous conditions, in the presence or absence of divalent cations (Zn2+, Ca2+, Cu2+, or Mg2+).

L16 ANSWER 23 OF 33 MEDLINE  
 ACCESSION NUMBER: 97277241 MEDLINE  
 DOCUMENT NUMBER: 97277241 PubMed ID: 9115446  
 TITLE: Solution structure of the sodium channel antagonist

**conotoxin GS**: a new molecular caliper for probing sodium channel geometry.  
 AUTHOR: Hill J M; Alewood P F; **Craik D J**  
 CORPORATE SOURCE: Centre for Drug Design and Development The University of Queensland, Brisbane, Queensland, 4072, Australia.  
 SOURCE: STRUCTURE, (1997 Apr 15) 5 (4) 571-83.  
 Journal code: 9418985. ISSN: 0969-2126.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: PDB-UNKNOWN  
 ENTRY MONTH: 199706  
 ENTRY DATE: Entered STN: 19970630  
 Last Updated on STN: 19970630  
 Entered Medline: 19970616

AB BACKGROUND: The venoms of *Conus* snails contain small, disulfide-rich inhibitors of voltage-dependent sodium channels. **Conotoxin GS** is a 34-residue polypeptide isolated from *Conus geographus* that interacts with the extracellular entrance of skeletal muscle sodium channels to prevent sodium ion conduction. Although **conotoxin GS** binds competitively with mu **conotoxin** GIIIA to the sodium channel surface, the two toxin types have little sequence identity with one another, and **conotoxin GS** has a four-loop structural framework rather than the characteristic three-loop mu-**conotoxin** framework. The structural study of **conotoxin GS** will form the basis for establishing a structure-activity relationship and understanding its interaction with the pore region of sodium channels. RESULTS: The three-dimensional structure of **conotoxin GS** was determined using two-dimensional NMR spectroscopy. The protein exhibits a compact fold incorporating a beta hairpin and several turns. An unusual feature of **conotoxin GS** is the exceptionally high proportion (100%) of cis-imide bond geometry for the three proline or hydroxyproline residues. The structure of **conotoxin GS** bears little resemblance to the three-loop mu **conotoxins**, consistent with the low sequence identity between the two toxin types and their different structural framework. However, the tertiary structure and cystine-knot motif formed by the three disulfide bonds is similar to that present in several other polypeptide ion channel inhibitors. CONCLUSIONS: This is the first three-dimensional structure of a 'four-loop' sodium channel inhibitor, and it represents a valuable new structural probe for the pore region of voltage-dependent sodium channels. The distribution of amino acid sidechains in the structure creates several polar and charged patches, and comparison with the mu **conotoxins** provides a basis for determining the binding surface of the **conotoxin GS** polypeptide.

L16 ANSWER 24 OF 33 MEDLINE  
 ACCESSION NUMBER: 96280640 MEDLINE  
 DOCUMENT NUMBER: 96280640 PubMed ID: 8688418  
 TITLE: Three-dimensional solution structure of mu-**conotoxin** GIIIB, a specific blocker of skeletal muscle sodium channels.  
 AUTHOR: Hill J M; Alewood P F; **Craik D J**  
 CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, Australia.  
 SOURCE: BIOCHEMISTRY, (1996 Jul 9) 35 (27) 8824-35.  
 Journal code: 0370623. ISSN: 0006-2960.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)



LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199608  
 ENTRY DATE: Entered STN: 19960911  
 Last Updated on STN: 19960911  
 Entered Medline: 19960826

AB The three-dimensional solution structure of mu-conotoxin GIIIB, a 22-residue polypeptide from the venom of the piscivorous cone snail *Conus geographus*, has been determined using 2D 1H NMR spectroscopy. GIIIB binds with high affinity and selectivity to skeletal muscle sodium channels and is a valuable tool for characterizing both the structure and function of these channels. Structural restraints consisting of 289 interproton distances inferred from NOEs and 9 backbone and 5 side chain dihedral angle restraints from spin-spin coupling constants were used as input for simulated annealing calculations and energy minimization in the program X-PLOR. In addition to the 1H NMR derived information, the 13C resonances of GIIIB were assigned at natural abundance, and hydroxyproline C beta and C gamma chemical shifts were used to distinguish between the cis and trans peptide bond conformations. The final set of 20 structures had mean pairwise rms differences over the whole molecule of 1.22 A for the backbone atoms and 2.48 A for all heavy atoms. For the well-defined region encompassing residues 3-21, the corresponding values were 0.74 and 2.54 A, respectively. GIIIB adopts a compact structure consisting of a distorted 310-helix, a small beta-hairpin, a cis-hydroxyproline, and several turns. The molecule is stabilized by three disulfide bonds, two of which connect the helix and the beta-sheet, forming a structural core with similarities to the CS alpha beta motif [Cornet, B., Bonmatin, J.-M., Hetru, C., Hoffmann, J. A., Ptak, M., & Vovelle, F. (1995) Structure 3, 435-448]. This motif is common to several families of small proteins including scorpion toxins and insect defensins. Other structural features of GIIIB include the presence of eight arginine and lysine side chains that project into the solvent in a radial orientation relative to the core of the molecule. These cationic side chains form potential sites of interaction with anionic sites on sodium channels. The global fold is similar to that reported for mu-conotoxin GIIIA, and the structure of GIIIB determined in this study provides the basis for further understanding of the structure-activity relationships of the mu-conotoxins and for their binding to skeletal muscle sodium channels.

L16 ANSWER 25 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE  
 5

ACCESSION NUMBER: 1996:57187 BIOSIS  
 DOCUMENT NUMBER: PREV199698629322  
 TITLE: Effect of OMEGA-conotoxin, a calcium channel blocker, on the circadian rhythm in rats.  
 AUTHOR(S): Masutani, Hideki; Matsuda, Yoshihiro; Nagai, Katsuya; Nakagawa, Hachiro  
 CORPORATE SOURCE: Div. Protein Metabolism, Inst. Protein Res., Osaka Univ., 3-2 Yamada-Oka, Suita, Osaka 565 Japan  
 SOURCE: Biological Rhythm Research, (1995) Vol. 26, No. 5, pp. 573-581.  
 ISSN: 0929-1016.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English

AB Using an Alzet osmotic minipump, we examined the effect of continuous infusion of SIGMA-conotoxin, a N-type voltage-sensitive calcium channel blocker, into the third cerebral ventricle above the suprachiasmatic nucleus (SCN) of the hypothalamus on the circadian drinking rhythm of rats

maintained under a 12-h light and 12-h dark **cycle** and constant darkness. SIGMA-**Conotoxin** (10<sup>-6</sup> mol/h) infusion disrupted the rhythm in both conditions. In contrast, infusions of nifedipine (10<sup>-4</sup> mol/h), a dihydropyridine sensitive L-type calcium channel blocker, did not eliminate the rhythm. These findings suggest that N-type voltage-sensitive calcium channels are involved in the mechanism of generation of the circadian rhythm driven by the circadian oscillator in the SCN.

L16 ANSWER 26 OF 33 MEDLINE DUPLICATE 6  
 ACCESSION NUMBER: 95380023 MEDLINE  
 DOCUMENT NUMBER: 95380023 PubMed ID: 7651585  
 TITLE: Characteristics of [125I]omega-**conotoxin** labeling using bifunctional cross **linker** DSP in crude membranes from chick brain.  
 AUTHOR: Ichida S; Wada T; Akimoto T; Kasamatsu Y; Tahara M; Hasimoto K  
 CORPORATE SOURCE: Department of Biological Chemistry, Faculty of Pharmacy, Kinki University, Higashi-Osaka, Japan.  
 SOURCE: NEUROCHEMICAL RESEARCH, (1995 Apr) 20 (4) 467-73. Journal code: 7613461. ISSN: 0364-3190.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199509  
 ENTRY DATE: Entered STN: 19951005  
 Last Updated on STN: 20000303  
 Entered Medline: 19950927  
 AB. Characteristic of [125I]omega-**conotoxin** (omega-CgTX) labeling using bifunctional cross **linker** (dithio bis[succinimidyl propionate]:DSP) was systematically investigated in crude membranes from chick whole brain. [125I]omega-CgTX specifically labeled 216 kDa as a main and 236 kDa as a minor bands in the crude membranes under non-reduced condition, but not labeled under reduced condition. We investigated the effect of various Ca channel antagonists on [125I]omega-CgTX labeling with DSP in detail, and found that there is a strong correlation between the effects of Ca channel antagonists on [125I]omega-CgTX labeling of the 216 kDa band and specific [125I]omega-CgTX binding. These results suggest that labeling of the 216 kDa band under non-reduced condition with [125I]omega-CgTX using DSP involves the specific binding sites of [125I]omega-CgTX, perhaps including one of the neuronal N-type Ca channel subunits in the crude membranes.

L16 ANSWER 27 OF 33 SCISEARCH COPYRIGHT 2003 ISI (R)  
 ACCESSION NUMBER: 95:103197 SCISEARCH  
 THE GENUINE ARTICLE: QD640  
 TITLE: CHARACTERISTICS OF SPECIFIC I-125 OMEGA-CONOTOXIN GVIA BINDING AND I-125 OMEGA-**CONOTOXIN** GVIA LABELING USING BIFUNCTIONAL CROSS-**LINKERS** IN CRUDE MEMBRANES FROM CHICK WHOLE-BRAIN  
 AUTHOR: ICHIDA S (Reprint); WADA T; AKIMOTO T; KASAMATSU Y; TAHARA M; HASIMOTO K  
 CORPORATE SOURCE: KINKI UNIV, FAC PHARM, DEPT BIOL CHEM, OSAKA, OSAKA 577, JAPAN (Reprint)  
 COUNTRY OF AUTHOR: JAPAN  
 SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA-BIOMEMBRANES, (26 JAN 1995) Vol. 1233, No. 1, pp. 57-67. ISSN: 0005-2736.

DOCUMENT TYPE: Article; Journal  
 FILE SEGMENT: LIFE  
 LANGUAGE: ENGLISH  
 REFERENCE COUNT: 39

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Characteristics of specific I-125-omega-conotoxin GVIA (I-125-omega-CgTX) binding and I-125-omega-CgTX labeling using bifunctional crosslinkers were systematically investigated in crude membranes from chick whole brain. Aminoglycosides and dynorphine A (1-13) inhibited the specific binding of I-125-omega-CgTX, but not that of the L-type calcium ion channel antagonist [H-3](+)PN200-110. It seems likely that the inhibitory effect of dynorphine A (1-13) does not involve kappa-opiate receptors, based on results with the opiate receptor antagonist naloxone and the kappa-opiate receptor agonist U50488H. Spider venom, Cd2+ and La3+ inhibited the specific binding of I-125-omega-CgTX, as well as that of [H-3](+)PN200-110. Various L-type Ca2+ channel antagonists did not affect the specific binding of I-125-omega-CgTX. I-125-omega-CgTX specifically labeled 135 kDa and 215 kDa bands in crude membranes under reduced and non-reduced conditions, respectively. The crosslinker disuccinimidyl suberate (DSS) yielded better I-125-omega-CgTX labeling than the other two crosslinkers tested. We investigated the effect of various Ca2+ channel antagonists on I-125-omega-CgTX labeling with DSS in detail, and found that there is a strong correlation between the effects of Ca2+ channel antagonists on I-125-omega-CgTX labeling of the 135 kDa band and specific I-125-omega-CgTX binding. These results suggest that aminoglycosides and dynorphine A (1-13) are specific inhibitors of specific I-125-omega-CgTX binding, and that labeling of the 135 kDa band with I-125-omega-CgTX using DSS involves the specific binding sites of (125)I-omega-CgTX, perhaps including one of the neuronal N-type Ca2+ channel subunits in the crude membranes.

L16 ANSWER 28 OF 33 MEDLINE

ACCESSION NUMBER: 95152384 MEDLINE  
 DOCUMENT NUMBER: 95152384 PubMed ID: 7849598  
 TITLE: A common structural motif incorporating a cystine knot and a triple-stranded beta-sheet in toxic and inhibitory polypeptides.  
 AUTHOR: Pallaghy P K; Nielsen K J; Craik D J; Norton R S  
 CORPORATE SOURCE: NMR Laboratory, Biomolecular Research Institute, Parkville, Australia.  
 SOURCE: PROTEIN SCIENCE, (1994 Oct) 3 (10) 1833-9.  
 Journal code: 9211750. ISSN: 0961-8368.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199503  
 ENTRY DATE: Entered STN: 19950322  
 Last Updated on STN: 20000303  
 Entered Medline: 19950313

AB A common structural motif consisting of a cystine knot and a small triple-stranded beta-sheet has been defined from comparison of the 3-dimensional structures of the polypeptides omega-conotoxin GVIA (Conus geographus), kalata BI (Oldenlandia affinis DC), and CMTI-I (Curcubita maxima). These 3 polypeptides have diverse biological activities and negligible amino acid sequence identity, but each contains 3 disulfide bonds that give rise to a cystine knot. This knot consists of a ring formed by the first 2 bonds (1-4 and 2-5) and the intervening

polypeptide backbone, through which the third disulfide (3-6) passes. The other component of this motif is a triple-stranded, anti-parallel beta-sheet containing a minimum of 10 residues, XXC2, XC5X, XXC6X (where the numbers on the half-cysteine residues refer to their positions in the disulfide pattern). The presence in these polypeptides of both the cysteine knot and antiparallel beta-sheet suggests that both structural features are required for the stability of the motif. This structural motif is also present in other protease inhibitors and a spider toxin. It appears to be one of the smallest stable globular domains found in proteins and is commonly used in toxins and inhibitors that act by blocking the function of larger protein receptors such as ion channels or proteases.

L16 ANSWER 29 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1992:526871 BIOSIS

DOCUMENT NUMBER: BA94:134946

TITLE: A NOVEL N18TG2 X MESENCEPHALON CELL HYBRID EXPRESSES PROPERTIES THAT SUGGEST A DOPAMINERGIC CELL LINE OF SUBSTANTIA NIGRA ORIGIN.

AUTHOR(S): CRAWFORD G D JR; LE W-D; SMITH R G; XIE W-J; STEFANI E; APPEL S H

CORPORATE SOURCE: DEP. NEUROL., BAYLOR COLL. MED., 6501 FANNIN NB302, HOUSTON, TEX. 77030.

SOURCE: J NEUROSCI, (1992) 12 (9), 3392-3398.

CODEN: JNRSDS. ISSN: 0270-6474.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB A dopaminergic neuroblastoma was derived using somatic cell fusion of rat embryonic mesencephalon cells and the murine neuroblastoma-glioma cell line N18TG2. The resulting interspecies hybrid, named MES23.5, has retained a stable phenotype and karyotype for a continuous culture period of 1 year. The hybrid exhibits several properties that suggest that the parent primary neurons originated in the substantia nigra. The cell line contains tyrosine hydroxylase, which is identifiable both by biochemical and immunological methods and synthesizes dopamine, but no other catecholamine. Additionally, the cell line expresses apparent voltage-gated CA2+ channels as measured by high-affinity .omega.-conotoxin binding. The MES23.5 .omega.-conotoxin receptors are of similar affinity class to those found in adult rat mesencephalon. No dihydropyridine receptors, as measured by PN200-100 ligand binding, are present. None of these properties are found in the N18TG2 parent. At least three neuronal features, namely, tyrosine hydroxylase, dopamine synthesis, and .omega.-conotoxin receptor expression, are quantitatively elevated after sustained treatment with cAMP analogs. The cell line expresses a complex range of neural properties found in the dopaminergic neurons of the substantia nigra, and may therefore be useful elucidating further details of their cell biology.

L16 ANSWER 30 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1990:80898 BIOSIS

DOCUMENT NUMBER: BR38:36488

TITLE: DIFFERENTIAL INHIBITION BY OMEGA CONOTOXIN OF CYCLIC GMP PRODUCTION IN CULTURED CEREBELLAR NEURONS.

AUTHOR(S): LYSKO P G; FEUERSTEIN G Z

CORPORATE SOURCE: DEP. NEUROL., USUHS, BETHESDA, MD. 20814.

SOURCE: 19TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, PHOENIX, ARIZONA, USA, OCTOBER 29-NOVEMBER 3, 1989. SOC NEUROSCI ABSTR, (1989) 15 (1), 354.

DOCUMENT TYPE: CODEN: ASNEE5.  
CONFERENCE  
FILE SEGMENT: BR; OLD  
LANGUAGE: English

L16 ANSWER 31 OF 33 MEDLINE DUPLICATE 7  
ACCESSION NUMBER: 88157228 MEDLINE  
DOCUMENT NUMBER: 88157228 PubMed ID: 2450305  
TITLE: Cyclic AMP facilitates slow-inactivating Ca<sup>2+</sup> channel currents expressed by Xenopus oocyte after injection of rat brain mRNA.  
AUTHOR: Kaneko S; Nomura Y  
CORPORATE SOURCE: Department of Pharmacology, Toyama Medical and Pharmaceutical University, Japan.  
SOURCE: NEUROSCIENCE LETTERS, (1987 Dec 16) 83 (1-2) 123-7.  
Journal code: 7600130. ISSN: 0304-3940.  
PUB. COUNTRY: Ireland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198804  
ENTRY DATE: Entered STN: 19900308  
Last Updated on STN: 20000303  
Entered Medline: 19880412

AB Properties of voltage-sensitive Ca<sup>2+</sup> channels expressed in the Xenopus oocyte after injection of rat brain mRNA were investigated using the whole-cell voltage-clamp method as depolarization-induced Ba<sup>2+</sup> current, IBa. The apparent decay profile of IBa was considered to be the sum of a transient current (tau approximately 0.4 s) and a more sustained current (tau approximately 4 s). The sustained component was isolated by a weak depolarization from -20 to 0 mV, only detected in the mRNA-injected cells, and rather sensitive to omega-conotoxin GVIA. Moreover, increases in cytosolic cyclic AMP caused potentiation of the long-lasting current. These results suggest that slow-inactivating states of transplanted Ca<sup>2+</sup> channels are preferentially modulated by cyclic AMP-dependent protein kinase.

L16 ANSWER 32 OF 33 HCAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1986:497955 HCAPLUS  
DOCUMENT NUMBER: 105:97955  
TITLE: Conotoxin MI(B)-related compounds  
INVENTOR(S): Sakakibara, Shunpei; Nishiuchi, Yuji  
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61005095	A2	19860110	JP 1984-123402	19840615
PRIORITY APPLN. INFO.:			JP 1984-123402	19840615

GI

H-Arg-Cys (Acm) -Cys-His-Pro-Ala-Cys (Acm) -Gly-

Lys-Asn-Tyr-Ser-Cys-NH<sub>2</sub> I

Boc-Lys (ClZ) -Asn-Tyr (Cl<sub>2</sub>Bzl) -Ser- (Bzl) -Cys (4-MeBzl) -NH<sub>2</sub> II

Boc-Arg (Tos) -Cys (Acm) -Cys (4-MeBzl) -His-Pro-Ala-Cys (Acm) -Gly-OH III

AB Muscle relaxant title compds. were prepd. via the usual peptide coupling procedures. E.g., the cyclic peptide I (Acm = AcNHCH<sub>2</sub>), prepd. via condensation of pentapeptide deriv. II (Boc = Me<sub>3</sub>CO<sub>2</sub>C, ClZ = o-ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>O<sub>2</sub>C, Cl<sub>2</sub>Bzl = 2,6-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>, Bzl = PhCH<sub>2</sub>) with octapeptide III (Tos = tosyl), was deprotected and **cyclized** to give Des-[Gly]-**conotoxin** M I(B), whose muscle relaxant activity was comparable to that of a tubocurarine deriv.

L16 ANSWER 33 OF 33 MEDLINE DUPLICATE 8  
ACCESSION NUMBER: 86130500 MEDLINE  
DOCUMENT NUMBER: 86130500 PubMed ID: 2868714  
TITLE: A rapid, sensitive mass spectrometric method for investigating microscale chemical reactions of surface adsorbed peptides and proteins.  
AUTHOR: Chait B T; Field F H  
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1986 Jan 14) 134 (1) 420-6.  
Journal code: 0372516. ISSN: 0006-291X.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198603  
ENTRY DATE: Entered STN: 19900321  
Last Updated on STN: 19950206  
Entered Medline: 19860314

AB A new mass spectrometric method for measuring the products of reactions of surface adsorbed peptides and proteins is described. The technique is rapid, convenient, and sensitive and provides detailed information concerning the molecular weights of the reaction products and the rate and extent of reaction. The properties of the technique are illustrated by an investigation of cleavage reactions of the disulfide bonds in bovine insulin, **cyclic** somatostatin, and **conotoxin** G1 utilizing the reducing agent dithiothreitol.